Citation:

Salas-Salvado J , Fernandez-Ballart J, Ros E, Martinez-Gonzalez MA, Fito M, Estruch R ,Corella D, Fiol D, Gomez-Gracia E, Aros F, Flores G, Lapetra J, Lamuela-Raventos R, Ruiz-Gutierrez V, Bullo M, Basora J, Covas M. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status; one-year results of the PREDIMED randomized trial. *Arch Intern Med.* 2008; 168(22):2449-2458.

PubMed ID: 19064829

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the 1-year effect on metabolic syndrome status of behavioral intervention with 2 high-fat Mediterranean diets (MedDiet), one supplemented with virgin olive oil (VOO) and another supplemented with mixed nuts, with that of advice on a low-fat diet in volunteers at high risk for cardiovascular disease (CVD); all diets were ad libitum.

Inclusion Criteria:

- Community-dwelling men, aged 55 to 80 years, and women, aged 60 to 80 years;
- Absence of prior CVD; and presence of type 2 diabetes mellitus and/or 3 or more CVD risk factors:
  - Current smoker,
  - Hypertension (blood pressure ≥140/90mmHg or treatment with antihypertensive drugs),
  - Low-density lipoprotein cholesterol level of 160 mg/dL or higher or treatment with hypolipidemic drugs, high-density lipoprotein (HDL) cholesterol level of 40 mg/dL or lower,
- Body mass index (kg/m^2) of 25 or higher, or
- Family history of premature CVD.
- Eligible candidates were also screened in a face-to-face interview and completed a 26-item medical/risk factor questionnaire.

Exclusion Criteria:

- A severe long-term illness;
- Drug or alcohol addiction;
- Body mass index of 35 or higher;
- History of allergy or intolerance to olive oil or nuts.

Description of Study Protocol:

Recruitment

- Participants were recruited into the PREDIMED (Prevencion con Dieta Mediterranea) trial between October 1, 2003,

and June 25, 2004.
- Potential candidates (n=1487) were selected by physicians at primary care centers affiliated with 10 teaching hospitals in Spain on the basis of the eligibility criteria.

Design: Randomized controlled trial

Blinding used (if applicable) Not used

Intervention (if applicable)

- The PREDIMED study is a large, parallel group, multicenter, controlled 4-year clinical trial with full details of the protocol published elsewhere.
- Participants were randomly assigned to 1 of 3 intervention groups: MedDiet with VOO(MedDiet+VOO), MedDiet with mixed nuts (MedDiet+nuts), and advice about a low-fat diet (control).
- Based on the initial 14-item questionnaire addressing individual adherence to the MedDiet, dieticians gave personalized dietary advice to participants in both MedDiet groups during a 30-minute session (how to increase the use of olive oil for cooking, increased consumption of fruit, vegetables, and fish; consumption of white meat instead of red or processed meat; preparation of homemade dishes and red wine of moderate consumption).
- Dietitians also gave quarterly, 60-minute group sessions for each MedDiet group with written materials on the MedDiet.
- Participants assigned to the MedDiet groups were given either free VOO (15 L for 3 months) or packets of mixed nuts (1350 g of walnuts[15 g/d], 675 g of hazelnuts[7.5 g/d], and 675g of almonds[7.5 g/d] every 3 months).
- The control diet participants received general oral and written recommendations to reduce all types of fat, but were not given individualized intervention.
- Energy restriction was not advised for any of the intervention groups.
- All participants had free and continuous access to their dietician throughout the study.
- At baseline, participants took a 137-item validated food frequency questionnaire and a validated Minnesota Leisure-Time Physical Activity Questionnaire.
- Anthropometric measures, blood pressure and fasting blood samples were taken at baseline and repeated at 1 year.
- Participants were identified as having metabolic syndrome (MetS) based on the Adult Treatment Panel (ATP) III criteria.

Statistical Analysis

- Analysis of variance and χ^2 tests were used to compare qualitative traits and means of quantitative variables, respectively, between intervention groups.
- Repeated-measures analysis of variance was used to examine changes of numerical variables between baseline and 1 year.
- Differences in the incidence of MetS development and reversion among treatment groups were assessed
- By using logistic regression analysis with models adjusted for sex, age, obesity status at baseline, and body weight change.
- Level of significance was set at $P<0.05$.

Data Collection Summary:

Timing of Measurements Baseline and 1 year follow up
Dependent Variables

- Prevalence of metabolic syndrome

Independent Variables

- MedDiet + VOO
- MedDiet + Nuts
- Control Diet

Control Variables

Description of Actual Data Sample:

Initial N N=1264

Attrition (final N): N=1224
Age Men, 55 to 80 years; Women, 60 to 80 years
Ethnicity Authors did not identify the ethnicity

Other Relevant Demographics Study groups were well balanced with respect to demographic characteristics, CVD risk factors, MetS features and medication usage
Anthropometrics Anthropometric measures were similar between the study groups.
Location Spain; Specific location information about the multi-centers used in this study are published elsewhere.

Summary of Results:

Other Findings

- One-year prevalence of high waist circumference, elevated triglycerides level, and high blood pressure were significantly reduced in the MedDiet+nuts group compared with the control group ($P<0.05$).
- The overall prevalence of MetS at 1-year was reduced by 6.7%, 13.7%, and 2.0% in the MedDiet+VOO, MedDiet+nuts, and control groups, respectively (MedDiet+nuts vs control diet, $P<0.05$).
- Incident MetS rates were not significantly different among groups (MedDiet +VOO, 22.9%; MedDiet +nuts, 17.9%; and control, 23.4%), whereas reversion rates were highest in the MedDiet+nuts group ($P<0.05$ vs control group).
- Compared with the control group, crude odds ratios (95% confidence intervals) for MetS reversion were 1.4 (0.9-2.1) and 1.7 (1.1-2.7) for the MedDiet+VOO and the MedDiet+nuts groups, respectively.

Author Conclusion:

The authors concluded that older participants at high risk for developing CVD who consumed a non–energy-restricted, traditional Mediterranean-style diet supplemented with 1 daily serving of mixed nuts for 1 year showed a reduction in the overall prevalence of MetS compared with participants given advice on following a low-fat diet.

Additionally, subjects in the MedDiet+VOO group showed a non-significant reduction in MetS prevalence.

Reviewer Comments:

- *Ethnicity of the population was not identified.*
- *The details of the PREDIMED (Prevencion con Dieta Mediterranea) Study, a multicenter, 3-arm, randomized clinical trial were published elsewhere, so it was unclear exactly where the treatment centers were located.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes

4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	No
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	No
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes

7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes